Docket No.2503-1148
PATENT
MAILSTOP AF

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of

Tiziano SCUBLA, et al. Conf. 6915

Application No. 10/534,867 Group 1621

Filed October 28, 2005 Examiner S. A. Witherspoon

A PROCESS FOR THE PURIFICATION OF ,14-BUTANEDIOL MONONITRATE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

April 30, 2008

Sir:

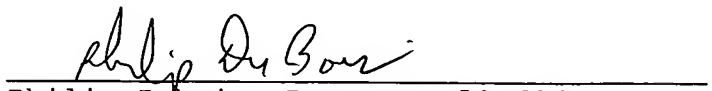
Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

A Notice of Appeal is filed herewith.

The review is requested for the reasons advanced on the attached sheets:

Respectfully submitted,

YOUNG & THOMPSON



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REASONS IN SUPPORT OF REQUEST FOR REVIEW

The present invention relates to a process for the purification of 1,4-butanediol mononitrate (BDMN) from 1,4-butanediol dinitrate (BDDN) and 1,4-butanediol (BD) in an efficient, easily controllable manner, which is safer for operators. In particular, the inventors of the present application have been the first to discover that BDMN can be separated from BD and BDDN in industrially advantageous yields by subsequent extractions with water and a water-immiscible organic solvent.

The sole remaining issue is whehter claims 1-10 and 12-21 are obvious under 35 U.S.C. § 103(a) in view of TREVES et al., DROUX et al., and Encyclopedia of Chemical Technology.

Applicants respectfully submit one skilled in the art interested in finding a method for the preparation of BDMN would not have substituted the flash chromatography taught by DROUX with the extraction techniques suggested by TREVES and Encyclopedia of Chemical Technology. Moreover, applicants respectfully submit that even if one skilled in the art were to combine the publications, the publications still would not result in the claimed invention.

TREVES is an article titled "*Henry's Law Constants of Some β-, γ-, and δ-Hydroxy Alkyl Nitrates of Atmospheric Interest*" from the Environmental Science & Technology Journal. The purpose of the article is to study organic nitrates that

form via a photodegradation of hydrocarbons in the troposphere in the presence of NO and NO_2.

TREVES indicates this process is an important area of study as it competes with the chemical cycle leading to ozone production. While TREVES does discuss synthetic methods to produce certain nitrates found in the atmosphere, TREVES does not discuss separating BDMN from BDDN and BD. Thus, there is no suggestion as to the need for a process for the purification of BDMN from BD and BDDN.

Rather, in an effort to remedy the deficiencies of TREVES for reference purposes, the Official Action cites to DROUX and the Encyclopedia of Chemical Technology.

DROUX is cited for the proposition that it is known that nitrooxy alcohols are produced by nitrating the corresponding diol with nitric acid in chloroform or trichloromethane, then separating the nitrooxy alcohol with an extraction of water and an organic chlorinated solvent in two consecutive extraction columns. DROUX also fails to discuss the need and difficulty in separating BDMN from BDDN and BD.

DROUX does not teach to separate and purify BDMN. Rather, DROUX teaches that one may prepare a mixture of diols which requires subsequent purification, i.e., by column chromatography. Indeed, DROUX is a common method for isolating a product from a reaction mixture, not a purification process (see Preparation 4, step B, on page 12). After quenching the chloroform reaction mixture with water, the aqueous phase is re-extracted with chloroform in order to recover all the organic compounds. This is confirmed in that the weight of the product

(4.26 g) obtained after complete evaporation of the solvent amounts to a yield higher than 100%. It is believed that the reason for such a yield is that the product recovered at the end of the work up is a mixture of mono-nitrate derivative (4-[[(nitro) oxy] methyl]] 2,2, diméthyl-cyclopropane-1-methanol and the corresponding di-nitrate derivative.

Therefore, the addition of water at the end of the reaction is only utilized to wash out the inorganic acidic compounds (nitric and acetic acids) generated as by products, while chloroform is added to recover all the mono-nitrate and di-nitrate end products.

Unlike step b) of the claimed process, the extraction of DROUX would not allow one to separate the mono-nitrate compound (i.e., BDMN) from the unreacted diol-compound (i.e., BD) to recover pure BDMN. Indeed, DROUX teaches that chromatography is necessary to purify the mono-nitro derivative. Thus, DROUX does not suggest the use of water-immiscible organic solvents to separate a mono-nitrate compound from an unreacted diol-compound and teaches away from the claimed invention which does not require the use of chromatography, especially claim 12.

Indeed, the first extraction of the organic mixture with water enables one to separate BD and BDMN (which are soluble in water) from BDDN, which remains in the organic layer, while the second extraction from the aqueous medium, performed with a water-immiscible organic solvent, enables one to separate BDMN from BD.

The final organic solution may contain BDMN with a purity of from about 99.5% to about 99.9%, in amounts from about

5% to about 8% w/w. As stated on page 8 of the description, the solution is substantially free from BDDN, whose amount is below 0.2%. BDDN is an explosive compound (i.e., even more so than BDMN). Therefore, keeping its levels as low as possible represents a further advantage of the invention.

Thus, with regard to the separation process taught by Droux it can be appreciated that Droux does not teach an actual purification technique, because only at the end of whole process the desired compound is purified by chromatography. The re-extraction with chloroform is performed only to obtain an organic solution containing most of the desired compound to be then submitted to purification by chromatography. In fact, according to this reference, the aqueous phase is re-extracted with chloroform and all the organic phases are combined, and then submitted to chromatography purification, for instance as per preparation 1 on page 9.

This stands in contrast to the claimed invention. In independent claims 1 and 12, the organic phase coming from the nitration reaction is first extracted with water and the desired product BDMN passes mostly in the aqueous phase, whereas BDDN byproduct remains in the organic phase. In the second extraction step, the aqueous phase is extracted with a water-immiscible organic solvent and product BDMN passes in the organic phase, whereas BD remains in the aqueous phase.

The Encyclopedia of Chemical Technology is cited for the proposition that extractions can be arranged in a counter-current manner. The publication discusses general principles of extraction and does not discuss separating BDMN from BDDN and

BD, or remedy any of the deficiencies of TREVES or DROUX for reference purpose.

Thus, none of the publications, alone or in combination, disclose or suggest purifying BDMN from BD and BDDN, why such a process is even needed, or that BDMN can be separated from BD and BDDN in industrially advantageous yields by subsequent extractions with water and a water-immiscible organic solvent as set forth in the claimed invention.

In view of the above, applicants respectfully request that the rejection be withdrawn.

Respectfully submitted,

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